

IN THE CLAIMS:

Please cancel claims 1-88. Please add new claims 89-178.

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89. (New). Adenovirus expressing a first protein which is selected from the group comprising an E1B protein and an E4 protein, prior to a second protein which is selected from the group comprising an E1A-protein.

90. (New). Adenovirus according to claim 89, characterised in that the first protein is an E1B protein, preferably an E1B55kd protein.

91. (New). Adenovirus according to claim 89, characterised in that the first protein is an E4 protein, preferably an E4orf6 protein.

92. (New). Adenovirus according to claim 89, characterised in that the E1A protein is an E1A12S protein.

93. (New). Adenovirus according to claims 89, 90, 91, or 92, characterised in that the first protein is a combination of E1B protein and E4 protein, preferably a combination of E1B55kD protein and E4orf6 protein.

94. (New). Adenovirus according to claim 89, characterised in that the adenovirus comprises at least one nucleic acid coding for a protein which is selected from the group comprising E1B proteins, E4 proteins and E1A proteins, whereby the at least one protein is under the control of a promoter which is different from the promoter controlling the expression of the protein in a wildtype adenovirus.

95. (New). Adenovirus according to claim 94, characterised in that the at least one protein is an E1B protein, preferably an E1B55kD protein.

96. (New). Adenovirus according to claim 94, characterised in that the at least one protein is an E4 protein, preferably an E4orf6 protein.

97. (New). Adenovirus according to claim 94, characterised in that the at least one protein is an E1A protein, preferably an E1A12S protein.

98. (New). Adenovirus according to claims 94, 95, 96, or 97, characterised in that the at least one protein is a combination of E1B protein and E4 protein, preferably a combination of E1B55kD protein and E4orf6 protein.

99. (New). Adenovirus according to claim 96, characterised in that the at least one protein is a combination of E1B protein and E1A protein, preferably a combination of E1B55kD protein and E1A12S protein.

100. (New). Adenovirus according to claim 96, characterised in that the at least one protein is a combination of E4 protein and E1A protein, preferably a combination of E4orf6 protein and E1A12S protein.

101. (New). Adenovirus according to claim 96, characterised in that the at least one protein is a combination of E1B protein, E4 protein and E1A protein, preferably a combination of E1B55kD protein, E4orf6 protein and E1A12S protein

102. (New). Adenovirus according to claim 96, characterised in that the expression of the E1B protein is controlled by a promoter, whereby the promoter is selected from the group comprising tumor-specific promoters, organ-specific promoters, tissue-specific promoters, heterologous promoters and adenoviral promoters, whereby the adenoviral promoter is different from the E1B promoter.

103. (New). Adenovirus according to claim 96, characterised in that the expression of the E4 protein is controlled by a promoter, whereby the promoter is selected from the group comprising tumor-specific promoters, organ-specific promoters, tissue-specific promoters, heterologous promoters and adenoviral promoters, whereby the adenoviral promoter is different from the E4 promoter.

104. (New). Adenovirus according to claim 102, whereby the adenoviral promoter is the E1A promoter.

105. (New). Adenovirus according to claim 96, characterised in that the expression of the E1A protein is controlled by a promoter, whereby the promoter is selected from the group comprising tumor-specific promoters, organ-specific promoters, tissue-specific promoters, heterologous promoters and adenoviral promoters, whereby the adenoviral promoter is different from the E1A promoter.

106. (New). Adenovirus according to claim 105, characterised in that the promoter controlling the expression of the E1A protein is YB-1 controlled or can be regulated by YB-1.

107. (New). Adenovirus according to claim 106, characterised in that the promoter controlling the expression of the E1A protein is the adenoviral E2 late promoter.

108. (New). Adenovirus according to claims 89, 90, 91, or 107, characterised in that the E4 protein, preferably the E4orf6 protein, and the E1B protein, preferably the E1B55kd protein, are under the control of the same or a common promoter.

109. (New). Adenovirus according to claim 89, characterised in that the adenovirus provides YB-1 in the nucleus through at least one adenoviral protein or that the provision of YB-1 in the nucleus is mediated through at least one adenoviral protein, whereby preferably the adenoviral protein is different from E1A.

110. (New). Adenovirus according to claim 89, characterised in that the adenovirus provides YB-1 for adenoviral replication through at least one adenoviral protein or mediates the provision of YB-1 for adenoviral replication

through at least one adenoviral protein, whereby preferably the adenoviral protein is different from E1A.

111. (New). Adenovirus according to claim 110, characterised in that the adenoviral protein is a complex of E4orf6 and E1B55kd.

112. (New). Adenovirus according to claim 89, characterised in that the nucleic acid of the adenovirus comprises at least one functionally inactive adenoviral region, whereby the region is selected from the group comprising the E1 region, the E3 region, the E4 region and combinations thereof.

113. (New). Adenovirus according to claim 112, characterised in that the region is the E1 region.

114. (New). Adenovirus according to claim 112, characterised in that the region is the E3 region.

115. (New). Adenovirus according to claim 112, characterised in that the region is the E4 region.

116. (New). Adenovirus according to claim 112, characterised in that the region comprises the E1 region, the E3 region and the E4 region.

117. (New). Adenovirus according to claim 89, characterised in that the adenovirus comprises at least one expression cassette, whereby the expression cassette comprises at least one promoter and a nucleic acid coding for an adenoviral protein, whereby the adenoviral protein is an E1B protein, preferably an E1B55kD protein.

118. (New). Adenovirus according to claim 117, characterised in that the promoter is different from the E1B promoter.

119. (New). Adenovirus according to claim 118, characterised in that the promoter is selected from the group comprising tumor-specific promoters, organ-specific promoters, tissue-specific promoters, heterologous promoters and adenoviral promoters, whereby the promoter is different from the E1B promoter.

120. (New). Adenovirus according to claim 89, characterised in that the adenovirus comprises at least one expression cassette, whereby the expression cassette comprises at least one promoter and a nucleic acid coding for an adenoviral protein, whereby the adenoviral protein is an E4 protein, preferably an E4orf6 protein.

121. (New). Adenovirus according to claim 120, characterised in that the promoter is different from the E4 promoter.

122. (New). Adenovirus according to claim 121, characterised in that the promoter is selected from the group comprising tumor-specific promoters, organ-specific promoters, tissue-specific promoters, heterologous promoters and adenoviral promoters, whereby the adenoviral promoters are different from the E4 promoter.

123. (New). Adenovirus according to claim 122, characterised in that the promoter is the E1A promoter.

124. (New). Adenovirus according to claim 89, characterised in that the adenovirus comprises at least one expression cassette, whereby the expression cassette comprises at least one promoter and a nucleic acid coding for an adenoviral protein, whereby the adenoviral protein is an E1A protein, preferably an E1A12S protein.

125. (New). Adenovirus according to claim 124, characterised in that the promoter is different from the E1A promoter.

126. (New). Adenovirus according to claim 125, characterised in that the promoter is selected from the group comprising tumor-specific promoters, organ-specific promoters, tissue-specific promoters, heterologous promoters and adenoviral promoters.

127. (New). Adenovirus according to claim 89, characterised in that the adenovirus comprises a nucleic acid, whereby the nucleic acid codes for YB-1.

128. (New). Adenovirus according to claim 127, characterised in that the nucleic acid coding for YB-1 is under the control of a promoter, whereby the promoter is preferably the E2 late promoter.

129. (New). Adenovirus according to claim 128, characterised in that the nucleic acid coding for YB-1 is under the control of a promoter, whereby the promoter is YB-1 dependent and YB-1 controlled, respectively.

130. (New). Adenovirus according to claim 127, characterised in that the nucleic acid coding for YB-1 is part of the expression cassette comprising a nucleic acid coding for an E1A protein, preferably a nucleic acid coding for an E1A12S protein.

131. (New). Adenovirus according to claim 130, characterised in that the nucleic acid coding for the E1A protein is separated from the nucleic acid coding for YB-1 through an IRES sequence.

132. (New). Adenovirus according to claim 89, characterised in that the nucleic acid coding for the E4 protein, preferably the E4orf6 protein, and the nucleic acid coding for the E1B protein, preferably the E1B55kD protein, are

contained in an expression cassette, whereby preferably the two coding sequences are separated through an IRES sequence.

133. (New). Adenovirus according to claim 132, characterised in that the promoter of the expression cassette is selected from the group comprising tumor-specific promoters, organ-specific promoters, tissue-specific promoters, heterologous promoters and adenoviral promoters, whereby the adenoviral promoters are different from the E4 promoter and different from the E1B promoter, preferably different from the wildtype E4 promoter and different from the wildtype E1B promoter.

134. (New). Adenovirus according to claim 89, characterised in that the adenovirus comprises an expression cassette comprising a promoter and a nucleic acid sequence, whereby the nucleic acid sequence is selected from the group comprising aptamers, ribozymes, aptazymes, antisense molecules and siRNA.

135. (New). Adenovirus according to claim 89, characterised in that the adenovirus comprises an expression cassette comprising a promoter and a nucleic acid sequence, whereby the nucleic acid sequence is a coding nucleic acid, whereby the nucleic acid codes for a molecule which is selected from the group comprising peptides, polypeptides, proteins, anticalines, antibodies and antibody fragments.

136. (New). Adenovirus according to claim 89, characterised in that the adenovirus comprises an expression cassette, whereby the expression cassette comprises a promoter and a nucleic acid sequence, whereby the nucleic acid sequence is selected from the group comprising apoptosis inducing genes, prodrug genes, protease inhibitors, tumor suppressor genes, cytokines and angiogenesis inhibitors.

137. (New). Adenovirus according to claim 89, characterised in that the adenovirus is a recombinant adenovirus.

138. (New). Adenovirus according to claim 89, characterised in that the adenovirus is an adenovirus mutant.

139. (New). Adenovirus according to claim 89, characterised in that the adenovirus is replication deficient.

140. (New). Adenovirus according to claim 139, characterised in that the adenovirus is capable of replicating in cells comprising deregulated YB-1 or having YB-1 in the nucleus.

141. (New). Adenovirus according to claim 140, characterised in that the cells contain YB-1 in the nucleus independent of the cell cycle.

142. (New). A nucleic acid coding for an adenovirus according to claim 89.

143. (New). A replication system comprising a nucleic acid according to claim 142 and a nucleic acid of a helper virus, whereby the nucleic acid of the helper virus comprises one or more of the expression cassettes of the adenovirus according to claim 89.

144. (New). A replication system according to claim 143, characterised in that the adenovirus or the nucleic acid coding therefor is lacking the expression cassette comprised by the helper virus.

145. (New). A vector comprising a nucleic acid according to claim 142 and/or a replication system according to claim 144.

146. (New). A vector according to claim 145, characterised in that the vector is an expression vector.

147. (New). A cell comprising an adenovirus according to claim 89 and/or a nucleic acid according to claim 142 and/or a replication system according to claim 142 and/or a vector according to claim 146.

148. (New). A cell according to claim 147, characterised in that the cell is a eucaryotic cell, preferably an animal cell, more preferably a mammalian cell.

149. (New). A cell according to claim 148, characterised in that the mammalian cell is a cell selected from the group comprising cells of mice, rats, guinea pigs, pigs, sheep, goats, cattle, horses, dogs, cats and human beings.

150. (New). A organism, preferably a mammal organism, comprising an adenovirus according to claim 89, a nucleic acid according to claim 142, a replication system according to claim 144, a vector according to claim 146, or a cell according to claim 149, whereby the organism is selected from the group comprising mice, rats, guinea pigs, pigs, sheep, goats, cattle, horses, dogs and cats.

151. (New). Use of an adenovirus according to claim 89, a nucleic acid according to claim 142, a replication system according to claim 144, a vector according to claim 146, or a cell according to claim 149, for replication of an adenovirus, preferably for *in vitro* replication of an adenovirus.

152. (New). Use of an adenovirus according to claim 89, a nucleic acid according to claim 142, a replication system according to claim 144, a vector according to claim 146, or a cell according to claim 149, for the manufacture of an adenovirus, preferably for *in vitro* manufacture of an adenovirus.

153. (New). Use of an adenovirus according to claim 89, a nucleic acid according to claim 142, a replication system according to claim 144, a vector according to claim 146, or a cell according to any of claim 149, for the expression of genes, preferably of genes which promote cell lysis, preferably cell lysis during adenoviral replication, and/or are promoting adenoviral mediated cell lysis.

154. (New). Use of an adenovirus according to claim 89, a nucleic acid according to claim 142, a replication system according to claim 144, a vector according to claim 146, or a cell according to claim 149, for the manufacture of a medicament.

155. (New). Use according to any of claims 151, 152, 153, or 154, characterised in that the cell in which the adenovirus replicates, has YB-1 in its nucleus, preferably has YB-1 in its nucleus independent of the cell cycle.

156. (New). Use according to claims 151, 152, 153 or 154, characterised in that the cell in which the adenovirus replicates, comprises deregulated YB-1.

157. (New). Use according to claim 154, characterised in that the medicament is for the treatment of tumor diseases.

158. (New). Use according to claim 157, characterised in that the tumor disease is selected from the group comprising malignant diseases, cancer, cancer diseases and tumors.

159. (New). Use according to claim 158, characterised in that the tumors are selected from the group comprising solid non-solid, malignant and benign tumors.

160. (New). Use according to claim 157, characterised in that at least a part of the tumor forming cells have YB-1 in the nucleus, preferably have YB-1 in the nucleus independent of the cell cycle.

161. (New). Use according to claim 157, characterised in that at least a part of the cells forming the tumor comprises deregulated YB-1.

162. (New). Use according to claim 157, characterised in that at least a part of the cells forming the tumor are Rb positive or Rb negative.

163. (New). Use according to claim 157, characterised in that at least a part of the cells forming the tumor have a resistance, preferably a multiple resistance against pharmaceutically active agents.

164. (New). Use according to claim 163, characterised in that the resistance is a multiple resistance.

165. (New). Use according to claim 163, characterised in that the resistance is against anti-tumor agents, preferably cytostatics, and/or that the resistance is caused by irradiation.

166. (New). Use according to claim 157, characterised in that the patient for which the medicament is intended, comprises a plurality of cells, whereby the cells are cells as described in claims 162, 163, or 164.

167. (New). Use according to claim 157, characterised in that the medicament comprises at least one further pharmaceutically active agent.

168. (New). Use according to claim 157, characterised in that the medicament is administered together with a further pharmaceutically active agent or is intended therefor.

169. (New). Use according to claims 167 or 168, characterised in that the further pharmaceutically active agent is selected from the group comprising cytokines, metalloproteinase inhibitors, angiogenesis inhibitors, cytostatics, tyrosine kinase inhibitors and cell cycle inhibitors.

170. (New). Use according to claim 157, characterised in that the medicament is administered prior, during or after irradiation.

171. (New). Use according to claim 170, characterised in that the irradiation is administered for the purpose of treating a tumor.

172. (New). Use according to claim 157, characterised in that the cell or the organism to be treated is subject to a measure, whereby the measure is selected from the group comprising irradiation, administration of cytostatics and hyperthermia.

173. (New). Use according to claim 172, characterised in that the measure is applied locally or systemically.

174. (New). Use according to claim 170, characterised in that the irradiation uses high-energy radiation, preferably uses any irradiation as used in the treatment of tumor diseases.

175. (New). Use of an adenovirus according to claim 89, a nucleic acid according to claim 142, a replication system according to claim 144, a vector according to claim 146, or a cell according to claim 149, or the manufacture of a medicament for the treatment of tumor diseases, characterised in that the tumor disease is selected from the group comprising breast tumors, bone tumors, gastric tumors, intestinal tumors, gall-bladder tumors, pancreas tumors, liver tumors, kidney tumors, brain tumors, ovarian tumors, skin tumors, tumors of

cutaneous appendages, head and neck cancer, uterine tumors, synovial tumors, laryngeal tumors, oesophageal tumors, lingual tumors, prostate tumors, preferably one of the preceding tumor diseases having the characteristics as described in claims 160 or 161.

176. (New). Use of an adenovirus according to claim 89, a nucleic acid according to claim 142, a replication system according to claim 144, a vector according to claim 146, or a cell according to claim 149, for the manufacture of medicament for the treatment of tumor diseases, whereby the tumor-specific promoter is a promoter which is specific for the tumor for which the medicament is used.

177. (New). Pharmaceutical composition comprising an adenovirus according to claim 89, a nucleic acid according to claim 142, a replication system according to claim 144, a vector according to claim 146 or a cell according to claim 149, and optionally a pharmaceutically acceptable carrier.

178. (New). Adenovirus according to claim 103, whereby the adenoviral promoter is the E1A promoter.